OFFICE OF THE PRIME MINISTER'S SCIENCE ADVISORY COMMITTEE

Professor Sir Peter Gluckman, KNZM FRSNZ FMedSci FRS
Chief Science Advisor

Speech at Auckland Medical Research Foundation: "Medical, life sciences and social sciences research: how they should be contributing to New Zealand's development"

Thursday 6 May 2010

PD Gluckman, Chief Science Advisor

Thank you for the opportunity to speak this evening. It is nine months since I took on the role of being the first Chief Science Advisor. Research is now being seen as being central to New Zealand's future development, and is one of the core components of a productivity agenda as announced by the Prime Minister at the opening of parliament earlier this year. And productivity is at the heart of ensuring not only our economic wellbeing but also our social and environmental wellbeing. There is not a challenge we face as a society that does not have science as a central part of its solution. Yet the paradox is that so many negative aspects of our modern condition reflect the impact of dealing with technology – be it the social and bullying pressures on our children that come from an over-connected electronic society or dealing with obesogenic environments or with the issues of climate change.

The simple fact is that for more than 30 years New Zealand has made a lesser investment in science than have other nations we would wish to be compared with. But that situation is changing. The changes made to the science system in the last year are the start of the most fundamental rethink in a generation about science and how it can best contribute to New Zealand. And medical science, using the broadest definition of such, is an important element in this rethink. In that last generation, our productivity has not risen at the rate that it should have. Relative to other countries in the OECD, our economic performance has fallen. There is an almost universal consensus from informed commentators that a significant investment in research and development is essential for a modern economy to grow and to sustain growth.

Most economies have targets for total public and private investment in R&D of the order of 3% of GDP – ours is only 1.2%. It is interesting that small but research-intensive countries like Singapore and Israel had the most resilient advanced economies in the recent recession. Indeed, such countries attribute their sustained growth through the period of the global economic downturn to their investment in research and development, which in each case started approximately 20 years ago. The problem for New Zealand is that we have not invested for a long time in R&D but investment returns from such expenditure takes 5-15 years to become obvious. That is why the Prime Minister is putting such a priority on improving the science system. New Zealand cannot be proud of its social circumstances. We have high rates of

Mail: PO Box 108-117, Symonds Street, Auckland 1150, New Zealand Physical: 2-6 Park Avenue, Grafton, Auckland 1023, New Zealand
Telephone: +64 9 923 1788 Facsimile: +64 9 373 7497 Website: www.pmcsa.org.nz Email: csa@pmcsa.org.nz

incarceration, we have health outcomes that are not as good as they should be, and our economic performance is not stellar. Economic growth is at the heart of improving our social circumstances, because we need growth to allow us to invest more in providing a better society and environment for New Zealanders. Equally, social development is at the heart of economic performance, because we need our population well educated, healthy and properly socialised.

One of my key roles as Chief Science Advisor is to work to improve the use of evidence in policy formation. Policy made in the absence of evidence is of course based solely on dogma and it is less likely to meet the results that its protagonists wish for. Evidence has to be good evidence if policy formation based on evidence is to be sound, and that requires sound scientific approaches. Policy made on bad evidence is no better than policy made on no evidence. I am currently drafting a report for the Prime Minister on ways in which the quality of evidence provision in policy formation can be enhanced. Evidence in turn requires quality research in all relevant domains, including the social science domain. Now I emphasize that evidence does not make policy – rather, it informs policy formation. There are many reasons why Governments can and should make policy decisions in the absence of evidence or even contrary to evidence. Whatever the evidence, in a democracy, Governments cannot go beyond the desire of the population. There are other reasons for diversion from the evidence, they may be fiscal, ideological or political.

Let me focus for a moment on social science. The issue of silos, which will be a constant theme in this talk, emerges. One of the problems in New Zealand is that we think that educational research is only about education, health research is only about health, and social welfare is only about social welfare, yet of course all of these and other domains interact. For example, policies about early childhood education are based on evidence within the educational domain. Yet there is a large body of research showing that early childhood education of the right type has in later life major influences on health, particularly mental health, major influences on the risk of criminality, and major influences on the risks of anti-social behaviours. Equally, there is a large body of evidence that shows that progress through adolescence is influenced by all sorts of experiences earlier in life, and whether one looks at the outcome of adolescence in terms of teenage pregnancy, suicide attempts, binge drinking, drug abuse, or inappropriate sexual behaviour, one comes to the conclusion that many different and apparently peripheral initiatives, for example in the areas of early childhood education and developing eusocial neighbourhoods, can have important influences in improving the transition to adulthood.

Yet we do not have the adequate capacity or the infrastructure to optimally integrate research activity across these domains. Indeed, we have rather poor social science research capacity and much of our public health research, while excellent, is seen in the very narrow domain of admittedly important medical issues, such as smoking or obesity. One of the challenges is how to improve our ability to integrate research across multiple domains. Beyond the need to improve the social and medical wellbeing of our population, we undertake research because we need economic prosperity, and we want to position ourselves well in this world. We will always have the danger as a little country of becoming irrelevant to the world. Science is one of the important ways in which New Zealand can maintain its relevance to the world. And indeed there is a new discipline emerging, that of science and diplomacy,

Mail: PO Box 108-117, Symonds Street, Auckland 1150, New Zealand Physical: 2-6 Park Avenue, Grafton, Auckland 1023, New Zealand
Telephone: +64 9 923 1788 Facsimile: +64 9 373 7497 Website: www.pmcsa.org.nz Email: csa@pmcsa.org.nz

where it is recognized that science has a very major part to play in maintaining and strengthening diplomatic relationships. Indeed in the last year I have found that science has a very important role to play in developing and maintaining international relationships – both with small countries like Singapore and with large countries like the United States. Medical research is one of those areas where we can play a particular role because we do have islands of real expertise that are well recognized internationally.

Now let me turn to the investment in medical research – where the investment gap is even more apparent. Expressed in terms of per-capita investment, for every dollar New Zealand spends on medical research from the public purse, you can see that Denmark spends 6 dollars, the United Kingdom spends 4.6 dollars (and of course this does not take into account the relatively similar expenditure by the Wellcome Trust), the United States spends 7.7 dollars, Singapore - a country we might compare ourselves to - spends 6.7 dollars and Australia spends about 2.7 dollars – and that does not take into account the large number of charities and regional trusts that operate within the Australian medical scene as well. But yet against this background, we really do have great medical research. Now let me emphasise that when I talk about medical research, I wish to use the broadest definition possible. It includes social science research, it includes clinical research, it includes public health research, and it includes bio-medical research both at the applied and the not yet applied ends of the spectrum. It is the broadest definitional canvas that you can think of.

The reason you will notice two things here – firstly I have carefully not used the words “basic” research or “blue-skies” research and have been somewhat reluctant to use the word “applied” research. The reason for that is that I think the words “blue-skies” and “basic” research have become pejorative in the minds of many New Zealanders because they fail to understand that there needs to be a balance of discovery type research and applied research and that to focus only on late-end applied research cannot not lead to a sustainable eco-system under which research can reach its full value and contribute to societal development, either socially or economically. In my own reports I am increasingly using the definitions of research used by the late Lord George Porter, a former President of the Royal Society of London. He said that there are only are two kinds of research – applied research and not yet applied research. The bottom line is that the complete science-based eco-system will be able to adopt virtually all knowledge in the general domain of medical research, broadly defined, to advance both the economy and the human condition. Indeed, studies have shown that in the biomedical domain, about half of applications are in areas other than those where the work started.

The second thing I do not want to do is to divide medical research into a series of silos such as public health research, bio-medical research, clinical research and so forth. The reason why I’m reluctant is that the New Zealand science system has become silo ridden and modern medical science is moving in the other direction. In large part this has occurred because of the small sums of money available to undertake research, which has led each silo to fight for its own piece of the cake. But in reality the future of research is based on integration, on multi-disciplinary approaches, on combined approaches to problem solving against a strategic background. Obesity will not be addressed by a simple public health approach any more than it will be addressed by a pure genetic or medical approach. We now know two things about obesity – that not everyone has the same sensitivity to an obesogenic environment and that we all now

Mail: PO Box 108-117, Symonds Street, Auckland 1150, New Zealand Physical: 2-6 Park Avenue, Grafton, Auckland 1023, New Zealand
Telephone: +64 9 923 1788 Facsimile: +64 9 373 7497 Website: www.pmcsa.org.nz Email: csa@pmcsa.org.nz

live in such an environment. Those differences in sensitivity are in part genetic and in part developmental. By some estimates over 50% of the risks of obesity are based in these causes of individual variation. But what is also clear from the study of the biology of obesity is that these very individuals are hard wired so that successful diet and exercise is for them very difficult – for such individuals a simple public health approach will not work. Tackling obesity requires a multi-dimensional approach based on a mix of public health measures and attention to individual differences. We have yet to learn how to exploit this emerging knowledge to help such individuals. For many the concept of blame is misleading – their biology is different and at the moment surgery remains their best solution.

But back to the issue of silos. The problem may be magnified in New Zealand because of the collective under-spend over many decades which has meant that researchers have tried to defend their turf. Because of this competition for funding we have more parochialism and more competition – often unacceptably aggressive competition – among scientists in New Zealand than is the case overseas. This has led, in my judgment, to a disproportionate amount of inappropriate behaviours in terms of the peer review system and there is a greater risk of committee bias than in larger systems. The peer review system is coming under increasing question worldwide given the increased pressures on scientists. Many small countries spend a lot more of their research effort on a less contestable system, for the simple reason that peer review at the entry point breaks down when the system is both small and tight. In turn this leads to a conservatism in what gets funded. All research requires peer review, but at what point and how that peer review occurs that is the issue. The largest medical research programme in the world does not use entry level peer review – that is the intramural programme of the NIH.

The CoREs represent an intermediate model in New Zealand. There was competition at entry but not at the level of the detailed science; large sums are distributed for intramural decision-making and peer review occurs at defined points post hoc. The CRI reforms also in part are aimed to address this issue. These are complex issues, and the status quo may remain not because it is best but because of the difficulties of alternatives. New Zealand is a biological economy. 60% of our exports come from agriculture, either directly or indirectly. And in the 1970s and 1980s much of the research that led to the strengthening of our agricultural science actually had its origins in biomedical research expertise, supported by organizations like the then Medical Research Council. Since that time the world has had the Human Genome Project, and then the development of genomics and the recognition of further layers of complexity of biological control at multiple levels, so-called epigenetics, are leading to a major revolution in our biological understanding. This type of knowledge is fundamental to our biological economy – think of the soil microbiome and nitrogen fixation, think of the ruminant gut microbiome and methane emissions, think of improving our forages for drought resistance, think of improving our animal production – and is also fundamental to our knowledge of human biology and disease causation and prevention.

Most, if not all, non-communicable disease is a function of an interaction between our environment – the very different ways we live, the very different social settings we live in, the very different foods we eat, our reproductive behaviours that are very different from those of a few generations ago – and our individual physiology. But that physiology is determined not just by our genome but overwhelmingly by

Mail: PO Box 108-117, Symonds Street, Auckland 1150, New Zealand Physical: 2-6 Park Avenue, Grafton, Auckland 1023, New Zealand
Telephone: +64 9 923 1788 Facsimile: +64 9 373 7497 Website: www.pmcsa.org.nz Email: csa@pmcsa.org.nz

our epigenome, which is the molecular reflection of the sum total of our experiences since we were conceived which alters the way our genes operate. The simplistic concept of gene-environment interactions and disease causation does not apply to disorders like cancer, heart disease, and diabetes. We are now facing the complexities of systems biology, which means that we have to integrate knowledge at the genetic, the epigenetic, the RNA, the cellular, the organismic and the social levels together if we are to make real progress against these diseases of an ageing population.

New Zealand needs to become better equipped to do such integrated research – it has not made the investments in infrastructure that are needed to be competitive. Yes, there are a small number of scientists working in particular niches who are making contributions, but if we really want significant involvement in solving these problems we need to do two things. First, we need to learn how to work collaboratively, both nationally and trans-nationally, so that we are in the partnerships that will make a real difference. Secondly, we need a strategic approach to investment. The infrastructure deficit is significant, and a coordinated plan for addressing it is essential. Talent capture is a further concern. These are now being addressed by high-level work programmes. It is only by getting access to new technologies and by working across boundaries that we will make the contributions to innovation that will on one hand solve many of these problems affecting our population but on the other lead to commercialisable opportunities. New Zealand's intellectual capacity in these areas is undoubted, but of the large number of New Zealand scientists who rely on international partnerships many could do much more if these relationships could be assisted and fostered better. These issues need to be addressed.

As I said at the start of this talk the primary reasons countries are investing more in R&D is for economic growth. When one stands back and looks at where New Zealand's opportunities for economic growth from knowledge are most likely, a few areas stand out. One is in the area of medical technology. There is no doubt that in areas like bioengineering, in terms of health software, in terms of device development, in terms of bio-electronics, there are a large number of outstanding New Zealand scientists. In places like the Auckland Bioengineering Institute, headed by Professor Peter Hunter, we have people whose reputation is at the highest worldwide.

We have a large unexploited asset. It is called our hospital system. We have one of the world's best health systems. We have more than 30 thousand doctors, nurses and other health professionals across our public health system, all of whom are capable of making highly innovative suggestions. We see our health system largely in terms of providing health services to our population, which is clearly its number one priority. But the investment in so many talented people and in an infrastructure of quality should be exploitable within certain limits – indeed it can improve the quality of care through staff empowerment. Already we have seen companies like Orion develop health services software which is being sold around the world. The experience of the National Health System innovations network in the UK shows both how a health system can be improved by a more innovative approach and how it can be used to develop new technologies, software, devices and in some cases systems and even drugs that can lead to significant export potential. The attitudinal change within the hospitals involved has been enormous. Already we are beginning to see new approaches along similar lines in places such as South Auckland. New Zealand's healthcare system is the ideal place in which to look for new ways to test new devices and new systems

Mail: PO Box 108-117, Symonds Street, Auckland 1150, New Zealand Physical: 2-6 Park Avenue, Grafton, Auckland 1023, New Zealand
Telephone: +64 9 923 1788 Facsimile: +64 9 373 7497 Website: www.pmcsa.org.nz Email: csa@pmcsa.org.nz

for export. All said and done, we are a small country in international terms but we have a complex healthcare technology and we should be able to use this to develop and test new healthcare systems. In other areas of medical science we equally have many opportunities.

Just a few random examples the work coming out of Dunedin on cancer diagnostics is clearly at the cutting edge. The longitudinal data base there has provided stellar information on human development. The modelling work of the Bioengineering institute in Auckland is at the cutting edge of modern systems biology. The Epigen consortium of AgResearch and the Liggins institute with international partners is at the cutting edge of modern nutritional science and has attracted enormous interest from commercial players. One does not have to look any further than the outstanding work of the Auckland Cancer Society Research Centre to realize that New Zealand can be the source of innovative drug discovery. The issue is how to exploit this. We have had a disappointing record in local development of drugs, not because we haven't had many good ideas, but because our capital markets have been small, because we have got caught in the trap of thinking that every drug needs to have its own little spin-out company, and because those companies have had relatively unsophisticated management and have been grossly undercapitalized.

We need to look for new ways of doing things in which we combine what limited expertise we have in technology transfer within New Zealand. We also need to partner at the pre-discovery stage internationally so we have access to better expertise, markets and capital. I've talked on this matter elsewhere. There are exploitable opportunities across the whole domain of medical research.

Researchers really need to be asking four questions of what they do although the weighting will be different depending on where the focus of activity is:

- Is it really good and innovative research –second rate research is really a waste of money
- What new knowledge will the world really gain from this research
- Can this new knowledge advance the public good
- What are the exploitable opportunities that might arise from this research?

Given our small size, the need to focus, these questions must be the basis of moving ahead. As the Minister said in release the strategic priorities document – Government funding will be based on excellence and impact.

But let me now turn to the issue of how we should do medical research in New Zealand. One kind of research which primarily lives within the universities and the hospitals is that which we do to encourage scholarship in general by supporting individual academics and doctors to undertake research. We do so largely to ensure quality of scholarship and clinical care. In many ways that is the kind of work that the foundations such as the Auckland Medical Research Foundation and Lottery Health support but it has also been a dominant part of the HRC portfolio. But the nature of medical science is rapidly changing. The 1980s and 1990s were a period of great excitement but also oversimplified conviction in biology. The explosion of molecular biology which culminated human genome project was the most obvious reflection of that period. The understanding of molecular biology at that time was linear – one gene led to the

Mail: PO Box 108-117, Symonds Street, Auckland 1150, New Zealand Physical: 2-6 Park Avenue, Grafton, Auckland 1023, New Zealand
Telephone: +64 9 923 1788 Facsimile: +64 9 373 7497 Website: www.pmcsa.org.nz Email: csa@pmcsa.org.nz

production of mRNA leading to the production of one protein. Disease was envisaged to largely be explained in terms of environmental factors or genetic factors and an enormous search went on for the genes for every disease with surprisingly disappointing results.

Indeed the major outcome of the human genome project was to challenge the whole basis of the science that set it up. We only have 20600 genes, just a thousand more than a flatworm – that clearly is not enough to explain the enormous number of biological functions. When the project started it was thought most of the DNA was junk – that is it did not do much. Now we know that most if not all DNA is functional but not leading to protein formation, but rather acts to regulate other parts of the DNA through a vast and ever growing complexity of RNA mediated regulation. We also know that DNA is effectively much more dynamic than we thought – copy number variation, non-genomic inheritance, allelic variation in epigenetic state, the role of epigenetic regulation. The conceptual implications of these advances take medical research into a new age.

Disease focused research now requires much more sophistication. Three modalities alone – the expansion of bioinformatics, epigenetics and genomics, the use of modern imaging modalities and the gut microbiome are changing the way we will address chronic disease cause, target identification and intervention. But each requires enormous data rich approaches, each requires major infrastructure, each requires multiple talents. A single experiment can produce millions of bits of data. Biology has become digital rather than analogue. Thus a new style of medical research is emerging – based on multidisciplinary approaches and operating not just in one lab but in multiple labs in multiple countries. Large consortia are forming. Europe has done this particularly well.

The challenge for medical research is how on one hand to break the challenge down into manageable bits but on the other to ensure the multilevel systems approach. Systems biology is now at the crux of medical research – layers of complex biochemistry mixed with enormous data bases and the science of bioinformatics – biology is becoming digital.

Gradually we are seeing changes in the way medical research is being conducted and funded. Bigger clusters, international networks, interdisciplinary teams. And all this creates a real challenge for New Zealand. We have tended to fund individuals and small groups, we have tended to work in independent groups rather than consortia and focus on small questions – some outstanding work has and continues to be done but the potential for impact has been variable. Medical research is generally done in the highly contestable and institutionally focused environment of universities – breaking down these boundaries is not easy. New Zealand needs to work out how it will take its research to scale. That involves real and virtual critical masses and better forms of collaboration across institutions – the Centres of Research Excellence represent an initial step in that direction. The need to form stable international partnerships of excellence is also apparent, and more effective forms of technology transfer and technology exploitation are required.

The world of medical research is changing – for New Zealand medical research to thrive it needs to be an integral part of this changed scene. This is not easy. How should we set priorities, how will we integrate

Mail: PO Box 108-117, Symonds Street, Auckland 1150, New Zealand Physical: 2-6 Park Avenue, Grafton, Auckland 1023, New Zealand
Telephone: +64 9 923 1788 Facsimile: +64 9 373 7497 Website: www.pmcsa.org.nz Email: csa@pmcsa.org.nz

what will have to be a mix of top down and bottom up approaches, does short term funding allow this kind of research, how do we ensure the innovative rather than the conservative gets funded, how do we ensure transfer to impact is rapid via policy, via health care and via economic exploitation. These are non-trivial questions. Governments properly need greater clarity as to the potential impact of research they fund be it in academic, social or health provision terms or in economic terms if they are to invest more. Government agencies increasingly have to justify their expenditure in strategic terms. We all know the Health Research Council is not as well-funded as similar agencies in our comparator nations. Why is that the case? Part of it is the general cultural issue that we have had about research in general. Part of it may be that health research has been primarily intertwined with academic and individualistic activity and thus the impact of the research effort *per se* is hard to see. Is the Health Research Council designed appropriately for the new age? For example the Health Research Council does not have economic objectives within its budget and this may have restricted how it is seen and what it does. As I have pointed out, much health and medical research can be seen through an economic lens.

Am I optimistic? Yes, I am. Because the dialogue has changed in tone, its nature is increasingly shifting from whether we *should* do research to *how* should we best do research for New Zealand's benefit. I believe that medical research is right at the heart of this and we should not be hesitant about it being a real investment. We need to do several things. We need to increase the volume of R&D, we need to build an infrastructure that is appropriate and modern, we need to develop funding tools that encourage collaboration both nationally and internationally rather than contestation, and we need to be far more aggressive in the international talent capture game. Too much of New Zealand's science system has had a focus on institutional heath and driving inter-institutional competition, rather than looking as a small country to combine our assets to compete on the world stage. We have to address this.

The Crown has started on a very determined path – my appointment, small but important increases in the science budget despite being a difficult year last year, the strategic priorities released by the Minister which made it clear that science was a central part of New Zealand's development plan, the CRI reforms, the restructuring of the Ministry. The Prime Minister understands that we are but at the start of a process.

The charitable sector is important at a number of points in the value chain – perhaps no more so than helping us recruit and retain the very best talent, because the international competition for talent is enormous. We have had 30 years of relative under-investment in knowledge, yet in that time some New Zealand medical scientists have done extraordinary things on extraordinarily small sums of money.

Thank you very much.

Mail: PO Box 108-117, Symonds Street, Auckland 1150, New Zealand Physical: 2-6 Park Avenue, Grafton, Auckland 1023, New Zealand
Telephone: +64 9 923 1788 Facsimile: +64 9 373 7497 Website: www.pmcsa.org.nz Email: csa@pmcsa.org.nz